Synta Pharmaceuticals and University of Toronto Researchers Elucidate Elesclomol Mechanism of Action Using Innovative Yeast-based Technology

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-Results support elesclomol results seen in human clinical trials-

-Elesclomol clinical trials on-going in acute myeloid leukemia and ovarian cancer-

LEXINGTON, Mass.--(BUSINESS WIRE)--Jan. 12, 2012-- Synta Pharmaceuticals Corp. (NASDAQ: SNTA) – A report published in the peer-reviewed journal PLoS ONE demonstrate how a novel yeast screening platform pioneered by researchers at the University of Toronto was used to elucidate the mechanism of action of elesclomol, a first-in-class drug that targets cancer cell metabolism and is currently being clinically developed by Synta Pharmaceuticals Corp. of Lexington, Massachusetts. Elesclomol is currently in clinical trials in both solid tumor and hematologic cancers, including a study in combination with paclitaxel in ovarian cancer and a single agent study in acute myeloid leukemia (AML) currently being conducted at Princess Margaret Hospital in Toronto.

“Elesclomol was previously shown to work by increasing the levels of reactive oxygen species to untenable levels causing cancer cell death, however details of how this occurs were unclear,” said Corey Nislow, Ph.D, Assistant Professor, Department of Molecular Genetics, University of Toronto. “It was critical to understand the mechanism of action of elesclomol because in clinical trials, a substantial subset of patients responded to treatment whereas others did not. Using our yeast-based chemogenomic screening platform and subsequent follow-up work in human cancer cells, we were able to clearly show that elesclomol works in the cell’s mitochondrion, where it interacts with the electron transport chain to cause rapid cell death. Our paper suggests that this interaction initiates redox reactions within the mitochondrion that induce a surge of reactive oxygen species resulting in cancer cell apoptosis. In clinical terms, this improved understanding of how elesclomol works has allowed Synta, the drug’s developer, to better select patients who may respond to this novel therapy in their on-going clinical trials.”

Dr. Nislow added that the collaboration involving the University of Toronto and Synta is an excellent example of leading academic institutions working closely with an innovative biotechnology company to support and accelerate the drug discovery process for the benefit of patients. The value of this research is being applied directly to the clinical development of elesclomol today.

“In three previous randomized trials, once-weekly dosing of elesclomol in combination with paclitaxel demonstrated clear evidence of activity in patients with low levels of serum lactate dehydrogenase (LDH), a biomarker associated with tumor hypoxia or low levels of oxygen,” said Vojo Vukovic, M.D., Ph.D, Chief Medical Officer, Synta. “The improved understanding of the mechanism of action of elesclomol based on the research conducted at the University of Toronto, and our ability to identify patients who are most likely to benefit from treatment suggests a potentially

wide application of elesclomol in a range of human cancers. The results which were published today allowed us to map a path forward in the clinical development of elesclomol both as a single agent and in combination with other anti-cancer agents."

About the Yeast-based Chemogenomic Screening Platform

The Nislow and Giaever labs at the University of Toronto have developed an automated drug interrogation platform that relies on the model organism, baker's yeast. Each gene in the genome of *Saccaromyces cerevisiae* has been systematically deleted and genetically bar coded with two DNA barcodes that allow rapid chemical screening against these mutants in parallel. These assays allow, in a single experiment, the identification of all genes required for survival in any condition (i.e. during drug treatment), resulting in a prioritized ranking of ALL genes according to how important they are for responding to the drug treatment. We have used this assay to understanding how thousands of compounds affect cell growth, including many FDA-approved drugs. More recently, the Nislow and Giaever labs have embarked on tackling promising drugs for which the exact mechanism of their action is not clear. These efforts are aided by virtue of the fact that thousands of "chemical genomic" drug signatures are held in the University of Toronto database against which novel compounds can be compared.

About Elesclomol

Elesclomol is a first-in-class, investigational drug candidate that triggers programmed cell death (apoptosis) in cancer cells through a novel mechanism: selectively targeting the electron transport chain in cancer cell mitochondria, disrupting cancer cell energy metabolism.

Mitochondria generate energy for cells, but also can induce apoptosis under certain conditions, such as a high level of oxidative stress. By sensitizing mitochondria and reducing barriers to apoptosis, elesclomol may provide a means to overcome resistance to traditional chemotherapy or targeted therapy.

Cancer cell mitochondria can be selectively targeted by elesclomol because cancer cell mitochondria are structurally and functionally different from their normal counterparts, making them more susceptible to changes to mitochondrial metabolism.

About Synta Pharmaceuticals

Synta Pharmaceuticals Corp. is a biopharmaceutical company focused on discovering, developing, and commercializing small molecule drugs to extend and enhance the lives of patients with severe medical conditions, including cancer and chronic inflammatory diseases. Synta has a unique chemical compound library, an integrated discovery engine, and a diverse pipeline of clinical- and preclinical-stage drug candidates with distinct mechanisms of action and novel chemical structures. All Synta drug candidates were invented by Synta scientists using our compound library and discovery capabilities. For more information, please visit www.syntapharma.com.

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Source: Synta Pharmaceuticals Corp.

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